

Covington & Burling Draft
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SUMMARY OF DATA ON L-ASPARAGINE MONOHYDRATE

Abstract. L-Asparagine monohydrate is a non-essential amino acid that occurs naturally in plants and animals. It is proposed for use in reaction flavors for smoking products. There is no available literature on its toxicology. However, it has been reported to stimulate ornithine decarboxylase activity by increasing the half-life of the enzyme. The thermal stability of L-asparagine is described in a Russian paper that has not yet been translated into English. *probably 8*

I. Background. L-Asparagine (Synonyms: α -aminosuccinic acid, aspartic acid β -amide, altheine, asparamide, agedoite) is a nonessential amino acid. It occurs both free and protein bound in all organisms. In plants, it occurs as a storage form, and in animals it occurs as a detoxification form of ammonia. Free L-asparagine occurs in plants and plant seedlings (e.g., asparagus). It has been isolated from sprouting vetch (*Vicia sativa* L., Leguminosae, Piria, 1848; Piutti, 1886; Chemical abstracts, 1925), from white lupine, and from soybean seedlings (Vickery et al., 1942).

A process has been developed by Avebe, a Dutch company, for producing this amino acid as a by-product in potato processing (Chem. Ind. 107: 527, 1984). The L-asparagine extracted from potato starch is 99 percent pure (dry weight).

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The FDA has approved the use of L-asparagine for use as a nutrient added to food provided that the final concentration of the chemical would be no more than 7 percent by weight of the total food protein, and other specifications are met (21 CFR § 172.320).

II. Use in Tobacco.

A. Function. L-Asparagine has been proposed for use in reaction flavors for smoking products, such as tobacco, reconstituted tobacco, or non-tobacco substitutes, which incorporate 0.001 percent to 5.0 percent by weight, based on the dry weight of the filler (Louise et al., 1981).

Information on the actual use of L-asparagine for this purpose is not available.

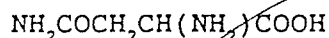
B. Use Level. The Industry maximum use level for L-asparagine monohydrate is 11-100 ppm.

III. Chemistry & Pyrolysis. The chemical synthesis of DL-asparagine starts with ethyl oxaloacetate (Cocker, 1940). The structure of asparagine was described by Steward and Thompson (1952). The physical and chemical properties of L-asparagine monohydrate are as follows:

Rel. mol. mass:	132.12 (without H ₂ O)
Density:	1.543 (at 15°C referred to water at 4°C)
Melting point:	234-235°C (bath preheated to 226°C)

Solubility: water: 0.95% w/w at 0°C 3.53%
at 28°C 52.75% at 100°C
ethanol, methanol, ether,
benzene: practically insoluble
pk: 2.02, 8.80
Appearance: orthorhombic bisphenoidal
crystals

STRUCTURE



and kinetics of dehydration

The thermal stability of L-asparagine ^{are} ~~is~~ described
in a Russian paper which has not been translated (Kalis et
al., 1989).

IV. Toxicology. There is no available literature
on the human health effects, acute toxicity, subchronic or
chronic toxicity, carcinogenicity, genotoxicity, reproductive
toxicity, teratology, or immunotoxicity of L-asparagine.

A. Metabolism. L-Asparagine is biosynthesized by
amidation of aspartate (asparagine-synthetase catalyzed), which
in turn is derived from oxaloacetate receiving the amino group
from glutamate in a transamination reaction.

The catabolism of L-asparagine is glucogenic. It is
hydrolyzed by asparaginase to ammonia and aspartate.

Aspartate is then transaminated to oxaloacetate or converted
into fumarate by the urea cycle. It forms metabolic
intermediates that can be converted into glucose or be
oxidized by the citric acid cycle.

B. Health Related Studies. L-asparagine has been reported to stimulate the activity of ornithine decarboxylase in cultured cells (Hogan and Murden, 1974; Chen and Canellakis, 1977), probably by increasing the half-life of this rapid turnover enzyme.

References

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